

words from about \$750 to about \$1400 per annum, with varying degrees of efficiency.

Our greatest need is financial assistance. The legislature of New Jersey, by an act approved April 20, 1906, appropriated a sum of money for purposes of general mosquito control, stating "provided that the aggregate sum appropriated for the purpose of this act shall not exceed three hundred and fifty thousand dollars."

A similar act in California, providing much less, would bring in return many times the original amount expended, through the stimulation of colonization alone in northern and central California. The readers of this article would be surprised to know how often the writer is requested on the part of prospective settlers to give information relative to the prevalence of malaria in certain parts of California and to state whether or not any effort is being made to control the same.

Several unsuccessful attempts have been made to pass legislative measures in this state. However, Tehama County has an exemplary ordinance directed against the *Anopheles* mosquito. A commendable feature about this ordinance is that it defines the term stagnant, viz., "The presence of the mosquito larva in said water shall be conclusive evidence that said water is stagnant," etc.

The several successful campaigns against malaria in California have shown how the attack can be made. We now need a larger, wider effort to drive the disease entirely outside the confines of the state, and this can be very largely accomplished in a relatively short time if systematic effort is put forth. As Californians we need not fear that this sort of publicity is poor advertising,—quite the contrary, any state will admit that it has mosquitoes and all will give highest praise to the state which frankly recognizes this defect and applies the means at hand to eliminate it. California has a decided natural advantage due to its largely semi-arid climate.

As a public health movement malaria control deserves the whole-hearted backing of the medical fraternity.

### DRUG ANAPHYLAXIS: AN ILLUSTRATIVE CASE?\*

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The literature of today contains many references and many articles on anaphylaxis. Dorland<sup>1</sup> defines it as: "The state of excessive susceptibility to the action of a toxin or a drug which sometimes follows infection or continued administration of the drug. Called also Theobald Smith phenomenon and hypersusceptibility."

Armond Deville<sup>2</sup>: "There exists a certain number of organic substances which introduced for the first time into the organism, in innocuous doses, have the property of producing in the organism, after a fixed period of incubation, anaphylaxis, that is, an extreme sensitiveness to minimum doses of the same substance which produce no trouble in an organism not so treated. This anaphy-

lactic condition appears to be connected with the development in the organism of a body, or a special property which exists, amongst others, in the serum of the blood since by introduction of this serum into another individual of the same species, this person is immediately plunged into a state of anaphylaxis."

Almost all experimental work and clinical observations have had to do with sera and serum reactions. A search of the literature reveals a scarcity of any article or case reports covering drug anaphylaxis.

F. Silvestri<sup>3</sup> observed cases of anaphylactic poisoning from various drugs, among which morphine is mentioned. He considers idiosyncrasy and true anaphylaxis one and the same thing, forming virulent and promptly acting poison out of proportion to the dosage.

The cause of death in true serum anaphylaxis is a stenosis of the pulmonary air passages. The period of time from the primary injections to the manifestations of symptoms of poisoning varies from six to twelve days after the second injection. Whether the same be true for drugs or not, is not known as we have no animal experiments to show.

Take the drug morphine, which is so often used in the treatment of spasmodic or bronchial asthma. The average lethal dose cannot be definitely determined, for what will be an ordinary dose for one individual, may be toxic for another.

Emerson<sup>4</sup> states: "In adults, not addicted to the drug, one to three grains will cause symptoms, often death. \* \* \* Fatal results have occurred even after the subcutaneous injection of  $\frac{1}{4}$  grain. People exhibit various degrees of susceptibility to the action of opium, so that it is impossible to say definitely what a fatal dose will be. Idiosyncrasy plays a large role in modifying the usual effects of opium, and may be of importance in medico-legal investigation \* \* \* Some diseases render the system very susceptible to its action."

Bronchial asthma per se, has a close relation to anaphylaxis, in its response in many persons to emanations from horses, its relation to hay-fever, etc., and is not considered here for the reason that it was not the cause of death, and the post-mortem findings showed nothing of particular value with reference to the cause of the asthmatic attacks. But the particular action of the drugs, the smallness of the lethal dose, the period of time over which it was given, the history of having been a morphine habitue in the past, leads us to consider this case as possibly one of drug anaphylaxis. Those who are frequently associated with morphine habitues tell of persons who, having been free from the drug for various periods of time, have often experienced marked toxic symptoms upon renewing the drug, even in very small doses, sometimes sudden death occurs.

In this connection, the following case is reported, hoping that it may be of slight value.

Unfortunately no serum tests were made, but the clinical symptoms lead us to the diagnosis, as well as the history of the case.

On Friday, May 22, 1914, at 8:40 A. M., was

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called to J. E. stating the trouble was spasmodic asthma. Getting there about 8:50 found a fairly healthy young woman with labored breathing and coughing in an attack of asthma. Tried to examine her heart but the rales in the chest overcame all sounds, except the first tone at the apex.

On questioning, she had been given doses of adrenalin hypodermically during the night by the husband, dosage ranging according to their statement from two to ten drops at a dose. Gave her fifteen drops of 1 to 1000 solution of adrenalin by dissolving of 3/200 grain tablet of adrenalin in 25 drops of water, at 9:00 A. M. After waiting 10 minutes, and getting no effect from this whatever, gave her a tablet containing 1/20 grain morphine nitrate, 1/50 grain nitro glycerine, 1/50 grain strychnia, together with 1/4 grain tablet morphine sulphate plain, hypodermically. At 9:40 no relief, so gave another 1/4 grain morphine with 1/150 of atropine, with fifteen drops of adrenalin solution that they had on hand. This made 11/20 of a grain of morphine that she had had in a half hour.

Stayed with the patient until a little after 10:00 o'clock. About 10:15 she had a good pulse, respirations were easy, pupils normal, was conscious and apparently in very good condition. Left four 1/4 grain hypo tablets of morphine sulphate plain, with instructions to use one at a time guarded with 15 minims adrenalin not oftener than every two hours, but not to use except during a severe paroxysm and not to start before evening.

Past History: She had been in the habit in past years to take morphine for the relief of her attacks of asthma, but had, according to her statement, taken none for two years. During this interval she had used the adrenalin solution with a hypodermic upon the advice of some physician. Two years ago she had been given, so they said, four grains of morphine in broken doses, before relief was obtained from a severe paroxysm. She was in a hospital at the time and on account of symptoms of morphinism had been given appropriate and successful treatment at once. They said she had had no morphine up to the time that I had administered it on this morning.

At 4:45 P. M. the husband telephoned that the wife had been asleep for over an hour. Upon asking if it were a normal sleep, he responded that it was, apparently. He stated that at 2:00 P. M. he had given her one of the 1/4 grain tablets that had been left and getting no result had repeated it at 2:30 upon her request. He said she vomited after the second dose and her bowels had moved with an enema. Asked him what the condition of her pupils was, and he replied, after examination, that they were pin-point, also that he was unable to rouse her by repeated shaking. Told him I would get there as soon as possible, but being delayed phoned him again and receiving the reply that she was in the same state, told him to make some strong black coffee and give to her if he could get her to swallow. Reached the house at 5:20, found her reclining in a chair, unconscious, pupils about one to two millimeters in diameter, slow, Cheyne-Stokes respiration, lips a peculiar brownish hue, face slightly flushed, pulse about 100—weak, easily compressed, but regular. One one-hundredth grain atropine was administered at once hypodermically, and an attempt made to wash the stomach, which was unsuccessful, on account of the tube being too soft.

The husband was informed that his wife was in a critical condition and that we might not be able to resuscitate her, phoned for an ambulance at 5:30 and got her into the receiving hospital by 5:45. She apparently died on the road to the hospital, although we had given the attendant some aromatic spirits of ammonia to hold to the nostrils on the trip.

At the hospital, artificial respiration by the Sylvester method and 1/50 grain of atropine administered. She gave one or two gasps while on

the table, although we could get no heart tones at all.

Autopsy held by Dr. Wagner, autopsy surgeon, the following day, showed: Throat negative so far as any abnormality. Chest: Lungs emphysematous with some thin bloody fluid. Heart absolutely normal. Abdomen: Stomach slightly injected mucosa. Intestines: Liver, spleen, kidneys, negative. Right ovary cystic, size large hen's egg. Left ovary beginning cystic degeneration. Uterus small, normal. The skin had a mottled reddish hue and on the arms were numerous old and new hypo pricks.

Diagnosis, overdose of morphine administered accidentally. COMMENTS: This case presents some rather interesting questions; first was there any idiosyncrasy for morphine on that particular date, or was the system so exhausted from the prolonged and labored efforts at breathing, that the morphine had a particularly toxic effect, or anaphylaxis.

With the history of having been a morphine habitue in the past and free from morphine for two years, could the dose of one grain of morphine at that particular time and in that particular individual have been more highly toxic than at any other time: again anaphylaxis.

She had all told 21/20 grains of morphine in a period of six hours as well as 1/150 grain of atropine.

From the foregoing, it is essential that a comparison be made between the manner of death from morphine and anaphylaxis. In anaphylaxis death, (serum anaphylaxis being considered, as we have no symptoms of drug anaphylaxis with death,) quoting from the experimental work of Auer and Lewis on guinea pigs, the respiratory movements cease before the heart stops beating, by several minutes. There is also a paralysis of the skeletal motor muscles, consciousness usually present to end. Autopsy findings in chest show lungs in a distended state, rather dry, and somewhat similar to emphysema. This latter condition according to Auer and Lewis<sup>5</sup>: "forms the anatomical basis for the explanation of immediate anaphylactic death, and that this asphyxia is produced by a stenosis of the pulmonary air passages." It is agreed by most observers that death is due to some disturbance in the medullary centers.

On the other hand, true acute morphine poisoning results according to Emerson<sup>4</sup>, Butler<sup>6</sup> and others "from true respiratory failure, the asphyxia being closely accompanied by cessation of the heart's action." There is cyanosis, contracted pupils, drowsiness, deepening into coma from which the patient cannot be roused, relaxation of the muscular system and abolition of the reflexes.

We have undoubtedly a case of true morphine poisoning, but the history, and the present attack taken together, leads us to consider seriously the possibility of drug anaphylaxis.

#### References.

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